REMARKS

Status of the Claims

Claims 23, 25-27, 30-34, 36, 38-48 and 50-61 are in the application.

Claims 23, 25-27, 30-34, 36, 38-48 and 50-61 have been rejected.

By way of this amendment, claims 25, 32, 42, 43, 45 and 50 have been amended, claims 59-61 have been canceled, and new claims 62-66 have been added.

Upon entry of this amendment, claims 23, 25-27, 30-34, 36, 38-48, 50-58 and 62-66 will be pending.

Summary of the Amendment

Claims 25, 32, 43, 45 and 50 have been amended to more clearly disclose embodiments of the invention. As amended, claims 25, 32, 43, 45 and 50 clearly recite that the fragments of peptides bind to ST receptors.

Claim 42 has been amended to more clearly disclose embodiments of the invention. As amended, claim 42 recites that the active agent is a therapeutic or imaging agent.

Claims 59-61 have been canceled as being directed to non-elected inventions.

New claims 62-66 correspond to claims 25, 32, 43, 45 and 50, respectively, but do not refer to SEQ ID NOs 55 and 56.

No new matter has been added.

Rejections under 35 U.S.C. §112, first paragraph

Written Description

Claims 23, 25-27, 30-34, 36, 38-48 and 50-58 have been rejected under 35 U.S.C: 112, first paragraph, as allegedly failing to comply with the written description requirement. It is asserted that specification does not demonstrate common structure and/or function for the claimed genus of pharmaceutical compositions and no representative number of species for the claimed genus is provided (Official Action, page 8). It is asserted that specification does not

provide a common core structure for ST or receptors that bind to (Official Action, page 9). Applicants respectfully disagree.

The claims have been amended to clearly reflect that the fragments of "peptides that bind to ST receptors" themselves bind to ST receptors. Accordingly, all antibodies and peptides that are claimed share the common function of binding to ST receptors. It is well settled that the structure of antibodies is sufficiently conserved such that reference to antibodies is compliant with the written description requirement. As for peptides, Applicants have disclosed over 50 species of the genus. Such disclosure is sufficient to establish that Applicants are in possession of the claimed invention. Moreover, fragments of specifically disclosed peptides which share the ST receptor binding function of such peptides have sufficient disclosure or structure and function to place them in compliance with the written description requirement.

As to the identity of ST receptors, at the time the application was filed, those having ordinary skill in the art would recognize that the reference to ST receptors was a reference to a specifically recognized protein. The ST receptor protein had been characterized at the time the present application was filed. In de Sauvage *et al.*, (*The Journal of Biological Chemistry*, Vol. 267, pp. 6479-6482 (1992), entitled: "Characterization of the Recombinant Human Receptor for Escherichia coli Heat-stable Enterotoxin"), the ST receptor was isolated and characterized after it had been cloned and sequenced in another article by the same group (*See*, .de Sauvage *et al.*, *The Journal of Biological* Chemistry, Vol. 266, pp. 17912-8 (1992), entitled: "Primary structure and functional expression of the human receptor for Escherichia coli heat-stable enterotoxin). Similarly, Currie, M. G. et al. (1992) Proc. Natl. Acad Sci. USA 89:947-951, which was incorporated in the specification by reference on page 14, lines 13-15, disclose that ST receptors were known as receptors which bind to heat stable enterotoxin ST. Currie refers to reference 5 which reports the cloning of the receptor. From the cloning, isolation, and characterization results reported by Currie and the two papers authored by de Sauvage *et al.*, it is clear that the identity of the protein referred to in the specification as the "ST receptor" was known to one of skill in the art at the time the invention was made. At the time the application was filed, the

identity of the intestinal protein which binds to heat stable enterotoxin was well established; the ST-receptor was known to be a specific and identifiable protein. Therefore, because the ST-receptor was well known in the art at the time the present application was filed, one of skill in the art would recognize that applicants were in possession of the invention at the time the application was filed.

In view of the foregoing, Applicant respectfully urge that the claims are in compliance with the written description requirement and respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Enablement

Claims 23, 25-27, 30-34, 36, 38-48 and 50-58 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. The c1aims allegedly contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Official Action states on page 14 that the specification, while being enabling for use in isolated cells, does not reasonably provide enablement for pharmaceutical uses in animals or humans. In asserting the claimed invention is not enabled by the specification, the evidence relied upon are the references Cianfrocca et al (British Journal of Cancer, 2006, pp 3 6), Russell Jones (Journal of drug Targeting, 12(2):113 123 2004), and El Andaloussi et al. (Current Pharmaceutical Design, 11:3597 3611, 2005).

These references, taken together, do not establish that those skilled in the art would question the asserted enablement of the claimed invention. Accordingly, the Office has not met its burden of establishing that those skilled in the art would not accept the objective truth of applicants' assertions that the claimed invention is enabled and the rejection should be withdrawn.

Cianfrocca et al is cited on page 15 as evidence that peptide drugs have limited success. Applicant urges that Cianfrocca et al supports a finding of enablement. The Office notes that Cianfrocca et al is not being relied upon to establish that peptide drugs do not work. Rather, the Office asserts that Cianfrocca et al raises the question of predictability of peptide drugs. Cianfrocca et al refers to results from a Phase I testing of a 5 amino acid anti-angiogenic peptide. Patients were deemed eligible if they were unresponsive to standard therapies or for which no therapies existed. Cianfrocca et al reported that one third of patients manifested prolonged stable disease. The authors conclude that the results were positive and that the drug should proceed with further clinical testing. The results in Cianfrocca et al reflect that the drug provided benefit a significant fraction of the patients tested, such patients having otherwise untreatable disease. Nothing in Cianfrocca et al supports a question of the enablement of the claimed invention. No drug can be expected to be effective for all patients and the standard for patentability has no such requirement.

Russell Jones is cited on page 16 as evidence that peptide drugs are not well suited for oral delivery. It is asserted that because the claims don't exclude oral delivery, issues raised by Russell Jones regarding limitations of delivering peptides orally provide evidence that the claimed invention is not enabled. Applicants respectfully urge that the position urged by the Office is without merit. Claim 41 refers to injectable forms of the claimed compositions. More importantly, there is no requirement that every drug be suitable for every route of administration.

El Andaloussi et al. is cited on page 16 as evidence that peptide drugs have delivery problems. The peptides in the present invention specifically bind to ST receptors. The problems outlined in El Andaloussi et al. are not present in the present invention and on the contrary, are addressed by the invention. The problems discussed in El Andaloussi et al. are specifically overcome by the nature of the invention. The citation of El Andaloussi by the Office is misplaced because El Andaloussi raises the question of peptides as drugs due to a problem of cell penetration. The peptides of the instant invention specifically bind to a receptor (ST receptor) on the cell membrane that is exposed to the outside of the cell. One skilled in the art recognizes that

ST receptors are cellular receptors and that the problems discussed in El Andaloussi are not issues in the enablement of the present invention. Applicant urges that El Andaloussi et al. does not support a finding of non enablement.

None of the references cited by the Office raise any specific issue of non enablement. Cianfrocca et al. refers to toxicity and adverse effects which exist at some level in nearly every drug and nothing in Cianfrocca et al. suggests that peptide drugs are particularly ineffective due to toxicity problems. On the contrary, Cianfrocca et al. disclose that the peptide they were studying had some limited effectiveness. Although all the effectiveness was quite limited and disappointing, it was sufficient to establish some small benefit which , while perhaps not significant for commercial viability nonetheless meets the requirements of enablement for patentability. Russell Jones refers to problems of oral administration of peptide drugs. The present invent]on is not so limited and, in fact, some of the claims specifically require that the claims be injectable. Russell Jones does not establish that peptides are not useful in pharmaceuticals, only that certain modes of administration are problematic. Accordingly, Russell Jones does not establish that claimed invention lacks enablement. El Andaloussi refers to problems of peptide drugs penetrating cells. The peptides used in the present invention are required to target proteins exposed to the outside of cells. The problems in El Andaloussi are specifically avoided by the present invention. When all of the references are taken together, they do not raise sufficient questions to doubt the objective truth of Applicant's assertion of enablement. On the contrary, one skilled in the art would be more likely to accept the objective truth of Applicant's assertion of enablement in view of the cited references.

The claims are in compliance with the enablement requirement of the first paragraph of 35 U.S.C. §112. Applicant respectfully requests that the rejection of claims 23, 25-27, 30-34, 36, 38-48 and 50-58 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement be withdrawn.

Rejection under 35 U.S.C. §103

Claims 42 and 57 have been rejected under 35 U.S.C. §103 as being unpatentable over Duflot (U,S. Patent No. 4,999,080) in view of Gluck (U,S. Patent No. 6,040,167).

Duflot discloses vaccines comprising a conjugated peptide that comprises heat stable enterotoxin linked to non-toxic carrier protein.

Gluck discloses liposomes.

It is asserted that it would have been obvious to combine the vaccines of Duflot with the liposomes of Gluck.

Claim 42 has been amended to recite that the active agent is a therapeutic or imaging agent. Neither Duflot nor Gluck teach or suggest conjugating heat stable enterotoxin to a therapeutic or imaging agent. Rather, Duflot proposes conjugation to a carrier which will increase the immune response against the conjugated compound, not conjugation to a therapeutic agent. Nothing in the combination of Duflot and Gluck teach or suggest the claimed invention.

Applicants respectfully request that the rejection of claims 42 and 57 under 35 U.S.C. §103 as being unpatentable over Duflot in view of Gluck be withdrawn.

Double Patenting Rejections

Claims 23, 25-28, 33, 34, 38 and 40 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5 and 6 of U.S. Patent No. 5,962,220.

Claims 23, 25-28, 33, 34, 38 and 40 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 7-10 and 13 of U.S. Patent No. 6,087,109.

Claims 23 and 28 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24, 26, 28, 29 and 33-41 of U.S. Patent No. 7,097,839.

Claims 23, 25-28, 33, 34, 38, 40, 41, 42, 45 and 47 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 10 and 12 of U.S. Patent No. 5,962,220 in view of Gluck.

As noted in previous responses, once claims have been indicated to be allowable, Applicants shall promptly provide Terminal Disclaimer as appropriate. To that end, the Examiner is invited to contact Applicants' undersigned representative and inform him of the allowability of the claims so that a Terminal Disclaimer can be promptly filed.

Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (610) 640-7855 if there are any questions regarding Applicants' claimed invention.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

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Attachments: de Sauvage *et al.*, (*The Journal of Biological Chemistry*, 267:6479-6482 (1992)
de Sauvage *et al.*, *The Journal of Biological* Chemistry, 266:17912-8 (1992)
Currie, M. G. et al. (1992) Proc. Natl. Acad Sci. USA 89:947-951